CLAIMS

1. Multilayer pharmaceutical form for controlled active ingredient release, comprising

a) a core layer comprising a substance having a modulating effect in relation to active ingredient delivery, where appropriate a core and/or an active ingredient,

b) an inner controlling layer which influences the delivery of the substance having a modulating effect and of the active ingredient which is present where appropriate from the core layer, comprising pharmaceutically usable polymers, waxes, resins and/or proteins,

c) an active ingredient layer comprising an active pharmaceutical ingredient and, where appropriate, a substance having a modulating effect,

d) an outer controlling layer comprising at least 60% by weight of one or a mixture of a plurality of (meth)acrylate copolymers composed of 98 to 85 C_1 to C_4 alkyl esters of (meth)acrylic acid and 2 to 15% by weight of methacrylate monomers with a quaternary ammonium group in the alkyl radical, and, where appropriate, up to 40% by weight of further pharmaceutically usable polymers,

where the layers may additionally and in a manner known per se comprise pharmaceutically usual excipients.

2. Multilayer pharmaceutical form according to Claim 1, characterized in that the core layer a) alternatively and essentially comprises the following ingredients:

I. a substance having a modulating effect, in crystalline, granular or coprecipitate form,

II. a substance having a modulating effect and an active ingredient, which may be present in successive layers in any sequence or in a mixture,

III. a neutral core (nonpareilles) coated with a substance having a modulating effect,

IV. a neutral core (nonpareilles) coated with a substance having a modulating effect and with an active ingredient, which may be present in successive layers in any sequence or in a mixture.

3. Multilayer pharmaceutical form according to Claim 1 or 2, characterized in that the inner controlling layer consists of a polymer which is insoluble in water or only swellable in water.

4. Multilayer pharmaceutical form according to Claim 3, characterized in that the polymer is selected from:

copolymers of methyl methacrylate and/or ethyl acrylate and methacrylic acid, copolymers of methyl methacrylate, methyl acrylate and methacrylic acid, copolymers of methyl methacrylate, butyl methacrylate and dimethylethyl methacrylate, copolymers of methyl methacrylate, ethyl acrylate and trimethylammoniumethyl methacrylate, copolymers of methyl methacrylate and ethyl acrylate, copolymers of ethyl acrylate, methyl acrylate, butyl methacrylate and methacrylic acid,

polyvinylpyrolidones (PVPs), polyvinyl alcohols, polyvinyl alcohol-polyethylene glycol graft copolymer (Kollicoat®), starch and derivatives thereof, polyvinyl acetate phthalate (PVAP, Coateric®), polyvinyl acetate (PVAc, Kollicoat), vinyl acetate/vinylpyrolidone copolymer (Kollidon® VA64), vinyl acetate: crotonic acid 9:1 copolymer (VAC: CRA, Kollicoat® VAC),

polyethylene glycols with a molecular weight above 1000 (g/mol), chitosan, a (meth)acrylate copolymer consisting of 20-40% by weight of methyl methacrylate and 60 to 80% by weight of methacrylic acid, a crosslinked and/or uncrosslinked polyacrylic acid, an Na alginate, and/or a pectin,

celluloses such as, for example, anionic carboxymethylcellulose and salts thereof (CMC, Na-CMC, Ca-CMC, Blanose, Tylopur), carboxymethylethylcellulose (CMEC, Duodcell®), hydroxyethylcellulose (HEC, Klucel), hydroxypropylcellulose (HPC), hydroxypropylmethylcellulose (HPMC, Pharmacoat, Methocel, Sepifilm, Viscontran, Opadry), hydroxymethylethylcellulose (HEMC), ethylcellulose (EC, Ethocel®, Aquacoat®, Surelease®), methylcellulose (MC, Viscontran, Tylopur, Methocel), cellulose esters, cellulose glycolate, cellulose acetate phthalate (CAP, Cellulosi acetas, PhEur, cellulose acetate phthalate, NF, Aquateric®), cellulose acetate succinate (CAS), cellulose acetate trimeliate (CAT), hydroxypropylmethylcellulose phthalate (HPMCP, HP50, HP55), hydroxypropylmethylcellulose acetate succinate (HPMCAS-LF, -MF, -HF).

5. Multilayer pharmaceutical form according to Claim 1 or 2, characterized in that the inner controlling layer consists of a wax such as, for example, carnauba wax and/or beeswax.

6. Multilayer pharmaceutical form according to Claim 1 or 2, characterized in that the matrix of the inner controlling layer comprises the resin shellac.

7. Multilayer pharmaceutical form according to Claim 1 or 2, characterized in that the inner controlling layer consists of a protein such as, for example, albumin, gelatin, gluten, collagen and/or zein.

8. Multilayer pharmaceutical form according to one or more of Claims 1 to 6, characterized in that the substance having a modulating effect has a molecular weight below 500 and is in solid form and is ionogenic.

9. Multilayer pharmaceutical form according to Claim 7, characterized in that substance having a modulating effect is soluble in water.

10. Multilayer pharmaceutical form according to Claim 7 or 8, characterized in that the substance having a modulating effect is an organic acid or the salt of an organic or inorganic acid.

11. Multilayer pharmaceutical form according to one or more of Claims 1 to 9, characterized in that the substance having a modulating effect is succinic acid, citric acid, tartaric acid, laurylsulphuric acid, a salt of these acids or a salt of the following anions: taurochlolate and other cholates, chlorides, acetates, lactates, phosphates and/or sulphates.

12. Multilayer pharmaceutical form according to one or more of Claims 1 to 10, characterized in that the active ingredient layer c) comprises metoprolol succinate, and the active ingredient release measured according to USP, 100 rpm, pH 6.8, is slower in the 2-hour intervals up to the fourth hour than in the 2-hour intervals from the fourth to the tenth hour.

13. Multilayer pharmaceutical form according to one or more of Claims 1 to 10, characterized in that the active ingredient layer c) comprises terbutaline sulphate, and the active ingredient release measured according to USP, 100 rpm, pH 6.8 is approximately constant in 2-hour intervals up to the twelfth hour.

14. Process for producing a multilayer pharmaceutical

form according to one or more of Claims 1 to 12 in a manner known per se by means of pharmaceutically customary processes such as direct compression, compression of dry, wet or sintered granules, extrusion and subsequent rounding off, wet or dry granulation or direct pelleting or by binding of powders (powder layering) onto active ingredient-free beads or neutral cores (nonpareilles) or active ingredient-containing particles or by means of spraying processes or fluidized bed granulation.

15. Use of a multilayer pharmaceutical form according to one or more of Claims 1 to 12 as ingredient of a multiparticulate pharmaceutical form, of pellet-containing tablets, minitablets, capsules, sachets, effervescent tablets or powders for reconstitution.